REMARKS

Claims 1-33 are pending in the present application. In response to the restriction requirement dated March 9, 2007, Applicant hereby provisionally elects, with traverse, to continue prosecution of the claims identified in Group I (claims 1-18). Per the Examiner's instructions, the Applicant further elects, with traverse, as follows: the species of No. A-8 (compounds that bind to Topo II and inhibit its activity), the species of No. B-1 (compounds that bind to HSP90 and inhibit its activity), the species of No. C-1 (cancer treatment), and the species of D-1 (sold tumors). The Applicant also reserves the right to later file one or more divisional applications directed to the subject matter of the non-elected claims.

The foregoing election notwithstanding, the Applicants respectfully traverse the restriction requirement, and respectfully requests reconsideration and withdrawal of the restriction requirement as set forth below.

On pages 4-5 of the Office Action, the Examiner alleges that there is no special technical feature linking the inventions of Groups 1-13, that defines a contribution over the prior art, as required by PCT Rule 13.2. However, to the contrary, the inventors have made a valuable contribution to the art by establishing that the first and second agents have synergistic effects on cancer treatment not previously shown or taught by the prior art.

The special technical feature that is common to the inventions of Groups 1-13 is that the inhibition of HSP90 increases the amount of Topo II available to bind to DNA, which is not shown or taught by Münster *et al.* (Clinical Cancer Res. 2001, 7:2228-

2236, IDS) ("Münster"). Münster does not show or teach the HSP90 inhibitor causing release of its client. Furthermore, nowhere in Münster is the term "topoisomerase II" used. Münster specifically describes doxorubicin as "a DNA-intercalating agent that acts on different phases of the cell cycle." However, topoisomerase II poisons specifically kill at the G2/M boundary, not throughout the cell cycle.

It is well known that doxorubicin has at least three distinct mechanisms of action on the cell. Alternatively, the mechanism of action is frequently quoted as unclear. The most common description of the mechanism of action of doxorubicin is as follows: doxorubicin damages DNA by intercalation of the anthracycline portion, metal ion chelation, or by generation of free radicals. Doxorubicin has also been shown to inhibit DNA topoisomerase II which is critical to DNA function. Therefore, Münster does not disclose the special technical feature of doxorubicin as modulating Topo II. It follows that the claims are unified by the concept that Topo II should be modulated in conjunction with HSP90 as a single inventive concept, in accordance with PCT Rule 13.1.

The mechanisms of action contemplated in Münster is intercalation. It would be well understood by one of skill in the art that doxobubicin acts as an intercalating agent that wedges between the bases of DNA and blocks DNA synthesis and transcription (*e.g.*, not dependent on Topoisomerase II action). Topoisomerase II is not involved in normal transcription and there are numerous enzyme involved in DNA synthesis, any of which could be the cause of halting the process. Acordingly, Münster does show or teach the unifying feature of the present invention, namely, the modulation of Topo II.

Thus, the Applicant respectfully submits that the special technical feature of the inventions of Group 1-13 constitutes a special technical feature as defined by PCT Rule 13.2 as it defines a contribution over the prior art.

For the foregoing reasons, the Applicants respectfully request that the Examiner withdraw the restriction requirement.

A favorable action on the merits is respectfully requested.

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Conclusion

This response is being submitted with a one-month extension. In the case any fee is owed, please charge deposit account number 03-3975 (ref. 67074-312021). If, for any reason, the Examiner finds the application other than in condition for allowance, the Examiner is requested to call the undersigned attorney at the Los Angeles telephone number (213) 488-7100 to discuss the steps necessary for placing the application in condition for allowance should the Examiner believe that such a telephone conference would advance prosecution of the application.

Respectfully submitted,

PILLSBURY WINTHROP SHAW PITTMAN LLP

Date: May 1, 2007

By: _____

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